

HARE. (H.A.)

*With the compliments
of the author.*

THE INFLUENCE OF ANTIFEBRIN, SALICYLIC ACID,
AND CARBOLIC ACID ON NORMAL AND AB-
NORMAL BODILY TEMPERATURE.

BY

H. A. HARE, M.D.,
(UNIV. OF PA.)

Demonstrator of Experimental Therapeutics and Instructor in Physical Diagnosis in the
University of Pennsylvania.

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THE INFLUENCE OF ANTIFEBRIN, SALICYLIC ACID, AND CARBOLIC ACID ON NORMAL AND AB- NORMAL BODILY TEMPERATURE.

SOME months since there appeared in the GAZETTE quite a lengthy study on fever, and the agents which produced and combated it, by Dr. Wood, Dr. Reichert, and myself, and the following series of experiments may in a manner be considered as a continuation of the former ones.*

At the time these experiments were begun no calorimetical investigations as to the manner in which these agents act had been performed, and it is only within the last few weeks that a short but elaborate paper has appeared in this journal on the influence of antifebrin on bodily heat by Dr. Evans, of Easton, Pa. With the exception of this last-named investigation the profession possesses the results of no true calorimetical observations on these three constantly used drugs, and it was this dearth of information which provoked these experiments.

The objects of the research have been, therefore, as follows:

First.—To determine the effect of each

* For the manner in which fever was produced, and any other details concerning the methods of this research, the writer must refer to the paper just mentioned.

The writer desires to call attention to the statement made in this joint paper that a thermogenic substance in the pepsin was a pepsin-peptone, as his researches make this somewhat doubtful. He has found that certain commercial pepsins charged with peptone fail absolutely to produce increase in bodily temperature, but, on the contrary, decrease it. This is of course in accord with the well-known fact that the commercial peptone of Grubler decreases animal temperature. It is plain that if the fever-producing agent really is a peptone, there must be two peptones in the commercial article, one of which decreases and the other increases bodily temperature. The relations of peptones to albumoses is so exceedingly close that it is quite probable that the so-called pepsin-peptone may be an albumose.

drug on normal temperature in the animal, which was free to come and go as it chose.

Second.—To discover what changes came about in the circulation during the alterations in the normal bodily temperature.

Third.—To determine what changes in the circulation occurred when the drug was influencing bodily temperature above normal.

Fourth.—To study in what manner these changes in temperature were produced, both with and without fever, or, in other words, whether these agents reduced bodily heat by altering heat production or dissipation, or both.

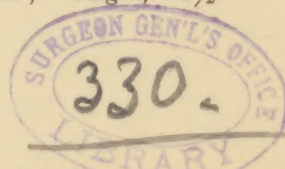
I. ANTIFEBRIN.

I have made ten experiments on the influence of antifebrin on normal rectal temperature, which show that this drug possesses to a marked degree the power of reducing bodily heat when no fever is present. In every instance there followed after the injection of the drug a very considerable fall, in some cases amounting to more than a degree Fahrenheit.

The following experiments, which agree in all respects with the others made on this point, will serve as examples:

Experiment 1. — Rabbit; weight, 2½ pounds.

Time.	Drug.	Rec. temp.
A.M.		
11.05		102½°
11.07	½ gr.	
11.27		102°
11.47		101°
12.07		101½°
12.27		101½°
12.47		101½°
1.07		103°



Animal very quiet.
Animal brisk as ever.

Experiment 2.—Rabbit; weight, $2\frac{1}{4}$ pounds.

Time. P.M.	Drug.	Rec. temp.
1.13		103°
1.15	$\frac{1}{2}$ gr.	
1.35		101 $\frac{2}{3}$ °
1.55		100 $\frac{4}{5}$ °
2.15		101 $\frac{3}{5}$ °
2.35		101 $\frac{3}{5}$ °
2.55		102°
3.15		102 $\frac{2}{5}$ °

Experiment 3.—Rabbit; weight, 2 pounds.

Time. P.M.	Drug.	Rec. temp.
1.05		102 $\frac{3}{5}$ °
1.07	$\frac{1}{2}$ gr.	
1.27		101°
1.47		101°
2.07		101 $\frac{2}{5}$ °
2.27		102°
2.47		102 $\frac{2}{5}$ °
3.07		102°

On studying the influence of antifebrin on bodily temperature and its relations to arterial pressure, we find that under normal conditions it generally produces a fall of temperature and a fall of pressure; but this is not by any means a constant action of the drug, since in Experiment 6 we see that though the temperature was decreased there was not a fall, but a rise of arterial pressure. This one exception would have but little weight against the others were it not that the fall of arterial pressure, when it did occur in the others, was not steady, but interrupted by temporary and unexplained rises; in other words, pressure and temperature did not fall side by side. Notwithstanding this fact, however, it is a just and proper conclusion that antifebrin in producing a lowering of temperature also acts as an arterial sedative.

Just here it may be well to call attention to the action which the drug possessed in Ex-

periment 7, namely, causing sudden cardiac failure from an unknown cause. In this experiment the animal died suddenly, so suddenly that the arterial pressure fell to zero from a considerable height in ten or fifteen seconds.

Death came without a tremor, a gasp, or any sign of an approaching cardiac failure.

On making an autopsy a small clot was found in the left ventricle, and there was also a long, well-formed clot extending from the canula in the carotid to the innominate artery.

The death was evidently due to this cause.

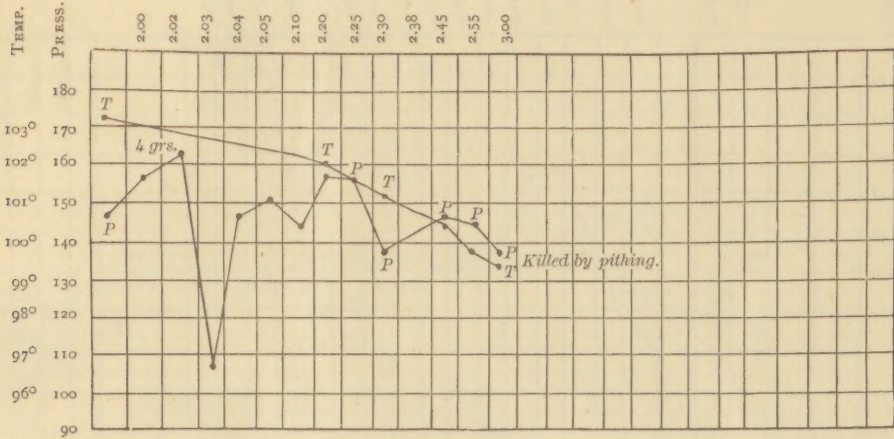
When antifebrin is injected into the jugular vein in an animal suffering from the pepsin fever it apparently has little, if any, effect on the pyretic condition, and both temperature and pressure mount upwards as if free from any inhibiting influence. This is the more remarkable since we have already discovered that this drug depresses normal temperature, but it may be that it is not able to cope with systemic changes produced by the pepsin. A glance at the charts will show this statement to be a fact, and we will now pass on to a consideration of its action on the production and dissipation of heat, hoping thereby to discover some cause for this rather remarkable result, for, as is well known, most drugs which depress normal temperature possess still greater powers over abnormal temperature.

From the experiments on heat production and dissipation in the normal animal we are able to draw the following conclusions, viz., that this drug reduces bodily temperature both by increasing dissipation and decreasing production. (See Experiments 12, 13, 14, and 15.)

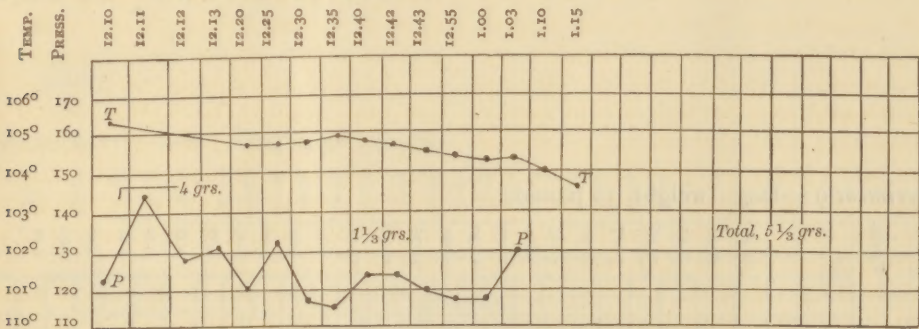
By the above the writer does not mean to insinuate that antifebrin decreases temperature by a double action necessarily in any one case, but rather that in one case the temperature is decreased by increased dissipation, and in another by decreased production.

Charts showing Arterial Pressure and its Relationship to Temperature, also the Fall of Temperature produced by Antifebrin.

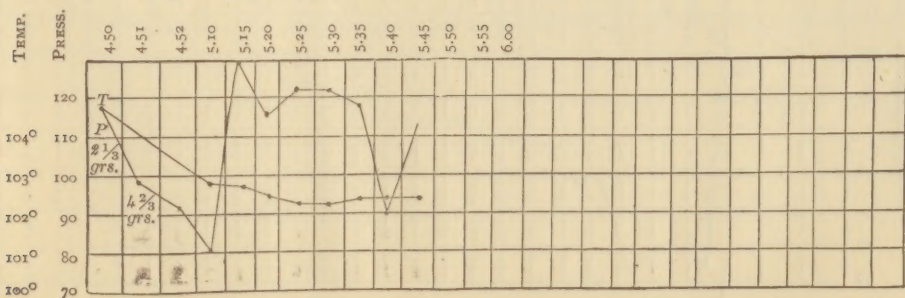
Experiment 4.—Dog; weight, 13 pounds.



Experiment 5.—Dog; weight, 32 pounds.

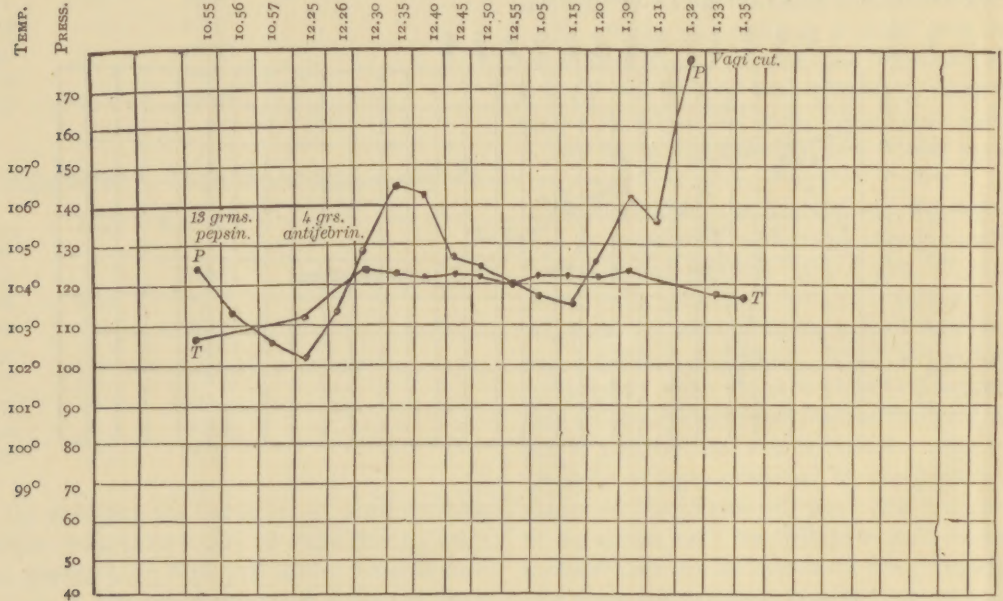


Experiment 6.—Dog; weight, 35 pounds.

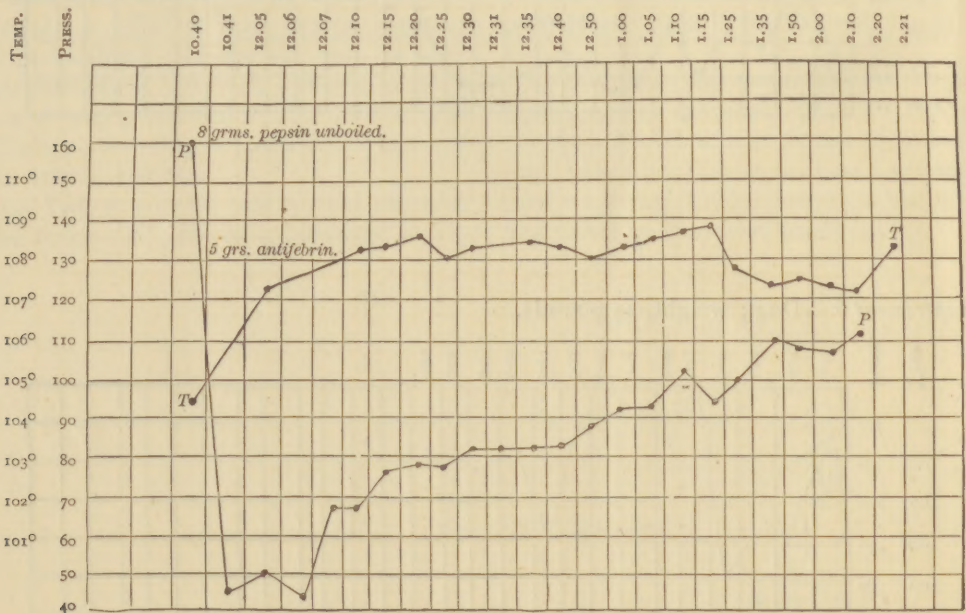


Charts showing Arterial Pressure and its Relationship to Temperature, also the ^{rise} ~~Fall~~ of Temperature ^{with} produced by Antifebrin in "Pepsin Fever."

Experiment 8.—Dog; weight, 30 pounds.

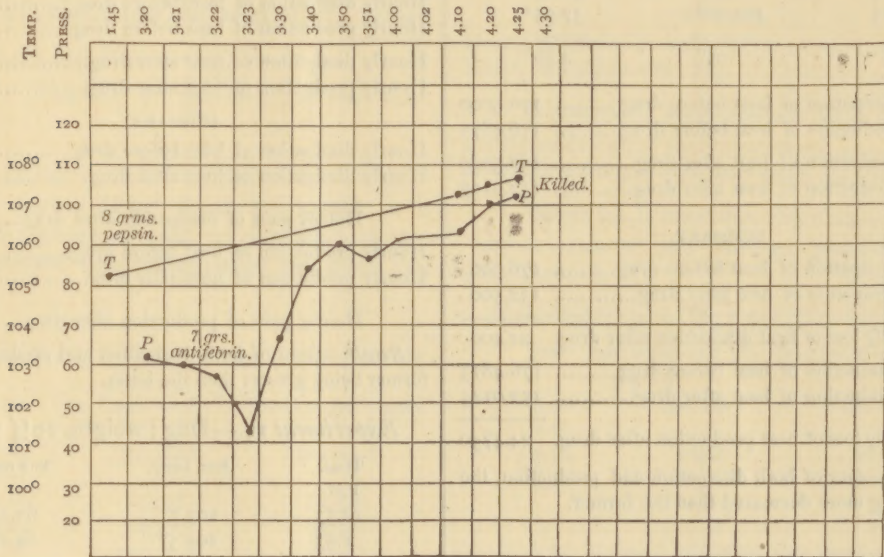


Experiment 9.—Dog; weight, 36 pounds.

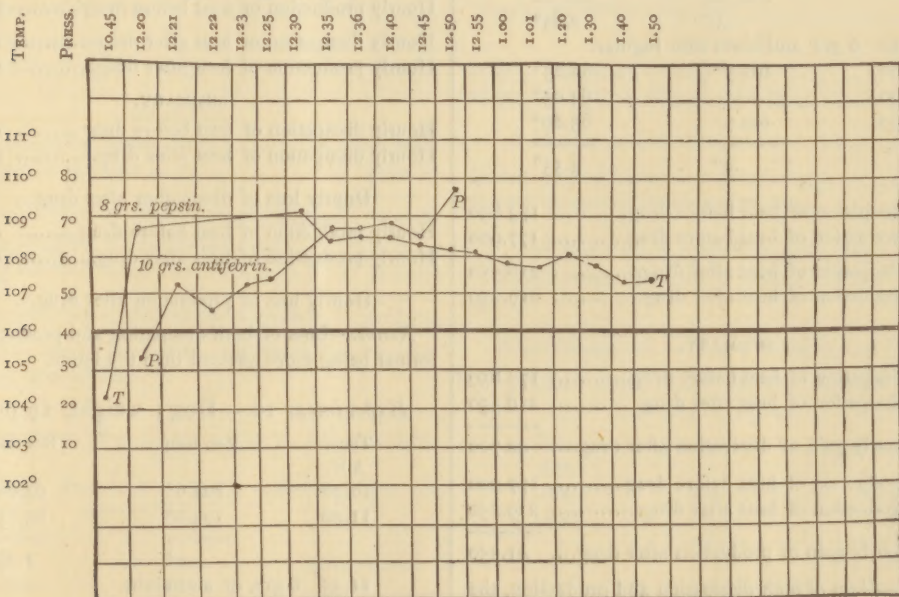


Charts showing Arterial Pressure and its Relationship to Temperature, also the ^{rise} ~~Fall~~ of Temperature produced by Antifebrin in "Pepsin Fever" (Continued).

Experiment 10.—Dog; weight, 25 pounds.



Experiment 11.—Dog; weight, 46 pounds.



Experiment 12.—Dog ; weight, 22 pounds.

Time. A.M.	Rec. temp.	Box temp.
9.00	105.30°	51.60°
10.00		53.05°
11.00	105.25°	54.50°
	.05°	2.90°
11.15	6 grs. antifebrin into jugular.	
11.15	104.25°	54.55°
12.15		56.15°
1.15	104.20°	57.05°
	.05°	2.50°

Hourly dissipation of heat before drug.....	176.9000
Hourly production of heat before drug.....	176.4875
Hourly dissipation of heat after drug.....	152.5000
Hourly production of heat after drug.....	152.0125

SUMMARY.

Hourly dissipation of heat before drug.....	176.900
Hourly dissipation of heat after drug.....	152.500
Hourly loss of heat dissipation after drug.	24.400
Hourly production of heat before drug.....	176.4875
Hourly production of heat after drug.....	152.0125
Hourly loss of heat production after drug.	24.4750

Result.—Loss of both dissipation and production, the latter being more decreased than the former.

Experiment 13.—Dog ; weight, 36 pounds.

Time. P.M.	Rec. temp.	Box temp.
1.20	102.7°	59.15°
2.20		
3.20	103.0°	62.00°
	.3°	2.85°
3.30	6 grs. antifebrin into jugular.	
4.00	102.5°	62.25°
5.00		64.05°
6.00	102.7°	65.80°
	.2°	3.55°

Hourly dissipation of heat before drug.....	173.850
Hourly production of heat before drug.....	177.900
Hourly dissipation of heat after drug.....	216.550
Hourly production of heat after drug.....	219.250

SUMMARY.

Hourly dissipation of heat before drug.....	173.850
Hourly dissipation of heat after drug.....	216.550
Hourly gain of dissipation after drug....	42.700
Hourly production of heat before drug.....	177.900
Hourly production of heat after drug.....	219.250
Hourly gain of production after drug....	41.350

Result.—Gain of both dissipation and production, the former being more increased than the latter.

Experiment 14.—Dog ; weight, 17 pounds.

Time. A.M.	Rec. temp.	Box temp.
10.25	103.0°	61.55°
11.25	104.2°	62.20°
	1.2°	.65°
11.35	6 grs. antifebrin into jugular.	
11.45	103.4°	62.15°
12.45	104.3°	63.30°
	.9°	1.15°

Hourly dissipation of heat before drug.....	79.300
Hourly production of heat before drug.....	94.600
Hourly dissipation of heat after drug.....	140.300
Hourly production of heat after drug.....	151.775

SUMMARY.

Hourly dissipation of heat before drug.....	79.300
Hourly dissipation of heat after drug.....	140.300
Hourly gain of dissipation after drug....	61.000
Hourly production of heat before drug.....	94.600
Hourly production of heat after drug.....	151.775

Hourly gain of production after drug.... 57.175

Result.—Gain of both dissipation and production, the former being greater than the latter.

Experiment 15.—Dog ; weight, 20¼ pounds.

Time. P.M.	Rec. temp.	Box temp.
12.53	103.7°	63.25°
1.53	104.5°	64.25°
	.8°	1.00°
2.00	6 grs. antifebrin into jugular.	
2.10	103.7°	64.25°
3.10	104.9°	65.15°
	1.2°	.90°

Hourly dissipation of heat before drug.....	122.000
Hourly production of heat before drug.....	134.156
Hourly dissipation of heat after drug.....	109.800
Hourly production of heat after drug.....	128.025

SUMMARY.

Hourly dissipation of heat before drug.....	122.000
Hourly dissipation of heat after drug.....	109.800
Hourly loss of dissipation after drug...	12.200
Hourly production of heat before drug.....	134.1500
Hourly production of heat after drug.....	128.0250

Hourly loss of production after drug... 6.1250

Result.—Loss of both dissipation and production, the former being more affected than the latter.

Experiment 16.—Dog ; weight, 19 pounds.

Time. A.M.	Rec. temp.	Box temp.
10.20	104.6°	64.60°
11.20	104.8°	65.85°
	.2°	1.25°
11.25	6 grs. of antifebrin.	
11.30	104.3°	65.65°
12.30	105.0°	66.90°
	.7	1.25°

Hourly dissipation of heat.....	152.500
Hourly production of heat	155.350
Hourly dissipation of heat after drug.....	152.500
Hourly production of heat after drug.....	162.475

SUMMARY.

Hourly dissipation of heat before drug.....	152.500
Hourly dissipation of heat after drug.....	152.500

Hourly dissipation after drug unchanged.

Hourly production of heat before drug.....	155.350
Hourly production of heat after drug.....	162.475

Hourly gain of production after drug.... 7.125

Result.—Dissipation not affected, but production increased.

The influence of antifebrin and thermogenesis during fever seems to consist in a lessened amount of heat production and also an increased heat dissipation on some occasions.

Experiment 17.—Dog ; weight, 17½ pounds.

10.40 Rec. temp. 103°. Injected 2 grs. pepsin.

Time.	Rec. temp.	Box temp.
A.M.		
11.10	105.3°	65.30°
12.10	105.0°	66.30°
	.3°	1.00°
12.13	6 grs. of antifebrin into jugular.	
12.15	105°	66.20°
1.15	102°	67.00°
	3°	.80°

Hourly dissipation of heat.....	122.0000
Hourly production of heat.....	119.0625
Hourly dissipation after drug	97.6000
Hourly production after drug.....	58.2250

SUMMARY.

Hourly dissipation before drug.....	122.0000
Hourly dissipation after drug	97.6000

Hourly loss of dissipation after drug... 25.4000

Hourly production of heat before drug.....	119.0625
Hourly production of heat after drug.....	58.2250

Hourly loss of production after drug... 60.8375

Result.—Loss of production and dissipation, the former being most affected.

Experiment 18.—Dog ; weight, 28½ pounds.

12.20 Rec. temp. 102.5°. Injected 2 grs. filtered pepsin.

Time.	Rec. temp.	Box temp.
P.M.		
1.20	105.3°	67.00°
2.20	105.2°	68.10°
	.1°	1.10°

2.35 8 grs. antifebrin into jugular.

Time.	Rec. temp.	Box temp.
P.M.		
2.45	105.3°	68.15°
3.45	105.1°	68.95°
	.2°	.80°

Hourly dissipation of heat.....	134.200
Hourly production of heat.....	132.070
Hourly dissipation of heat after drug.....	97.600
Hourly production of heat after drug	93.330

SUMMARY.

Hourly dissipation before drug.....	134.200
Hourly dissipation after drug.....	97.600

Hourly loss in dissipation after drug.... 36.600

Hourly production of heat before drug.....	132.070
Hourly production of heat after drug.....	93.330

Hourly loss in production after drug.... 38.740

Result.—Loss of both functions, production being most decreased.

Experiment 19.—Dog ; weight, 18½ pounds.

3.00 Rec. temp. 103.3°. Injected 2 grs. filtered pepsin.

Time.	Rec. temp.	Box temp.
P.M.		
3.50	104.8°	68.75°
4.50	105.1°	69.20°
	.3°	.45°
4.53	6 grs. of antifebrin into jugular.	
4.55	105°	69.00°
5.55	104°	69.70°
	.1°	.70°

Hourly dissipation of heat.....	54.9000
Hourly production of heat.....	59.0625
Hourly dissipation after drug.....	85.4000
Hourly production after drug.....	71.5250

SUMMARY.

Hourly dissipation of heat before drug.....	54.9000
Hourly dissipation of heat after drug.....	85.4000

Hourly gain of dissipation..... 30.5000

Hourly production of heat before drug.....	59.0625
Hourly production of heat after drug.....	71.5250

Hourly gain of production after drug... 12.4625

Result.—Gain of both functions, chiefly of dissipation.

Experiment 20.—Dog ; weight, 15 pounds.

10.20 Rec. temp. 103.5°. Injected 1½ grs. pepsin in jugular.

Time.	Rec. temp.	Box temp.
A.M.		
10.45	104.6°	67.40°
11.45	104.5°	68.40°
	.1°	1.00°
11.48	5 grs. of antifebrin into jugular.	
11.50	104.6°	68.50°
12.50	105.0°	69.40°
	.4°	.90°

Hourly dissipation of heat.....	122.0000
Hourly production of heat.....	120.8750
Hourly dissipation of heat.....	109.8000
Hourly production of heat.....	114.3000

SUMMARY.

Hourly dissipation of heat before drug.....	122.0000
Hourly dissipation of heat after drug.....	109.8000

Hourly loss of dissipation after drug... 12.2000

Hourly production of heat before drug.....	120.8750
Hourly production of heat after drug.....	114.3000

Hourly loss of heat production after drug. 6.5750

Result.—Loss of both functions, dissipation being decreased the most.

Experiment 21.—Dog; weight, 24 pounds.

10.30 Rec. temp. 103°. Injected 3 grs. filtered pepsin.

Time.	Rec. temp.	Box temp.
A.M.		
11.10	103.7°	61.25°
12.10	105.2°	62.55°
	1.5°	1.30°
12.25	Injected 6 grs. of antifebrin into jugular.	
12.30	105.0°	62.35°
1.30	105.3°	63.60°
	.3°	1.25°

Hourly dissipation of heat.....	158.600
Hourly production of heat.....	185.600
Hourly dissipation of heat after drug.....	152.500
Hourly production of heat after drug.....	157.920

SUMMARY.

Hourly dissipation of heat before drug.....	158.600
Hourly dissipation of heat after drug.....	152.500

Hourly loss of dissipation after drug.... 6.100

Hourly production of heat before drug.....	185.600
Hourly production of heat after drug.....	157.920

Hourly loss of production after drug.... 27.680

Result.—Loss of both functions, production being greatly decreased.

CONCLUSIONS.

1. *Antifebrin* effects marked depression of normal bodily temperature.

2. During the depressing action of antifebrin on normal temperature it seems to cause a slight fall in arterial pressure, although this is by no means a constant result, as it may cause a rise.

In the opinion of the writer, however, this drug in lowering temperature acts as an arterial sedative.

3. Notwithstanding the fact that antifebrin influences to such a marked degree normal bodily heat, it seems to possess little power

against the pyrexia produced by the introduction of pepsin into the blood, since under these circumstances the hitherto depressed pressure rises, as does also the bodily heat.

This curious fact must depend on some organic changes produced by the digestive ferment.

4. This drug reduces *normal* temperature apparently by influencing both production and dissipation.

5. Antifebrin in fever chiefly reduces the high temperature by decreasing heat production, and is therefore a valuable antipyretic.

II. SALICYLIC ACID.

IN ten experiments as to the influence of salicylic acid on the normal rectal temperature of the rabbit, the following results were obtained: In six experiments there was quite a marked fall of bodily temperature. In two others it rose slightly, while in the remaining two there was no change of any moment whatsoever. The writer is unable to give any explanation of these somewhat varying results, although one of them may be possibly explained by the struggling which took place when the animal was picked up. It may be, too, that in the remaining experiments the drug failed to reach the general system owing to delayed absorption, since, although an endeavor was made to place the hypodermic needle in the same region in each animal, it is perfectly possible that in one or two instances the drug may have entered in a spot where absorption went on slowly. That the drug does reduce normal bodily temperature seems proven not only by the majority of these experiments, but also by the results which were obtained in the experiments on the circulation and temperature in the dog. Thus we find on looking at the charts that in all five experiments on the normal animal when attached to the manometer there was a very marked fall in the temperature of the body.

These results are directly opposed to those obtained by Prof. Sée* and Fürbringer,† the first of whom used enormous doses, as much as 150 grains for a man, without finding any change in his temperature.

Prof. Sée gave the drug by the stomach, and, as Kohler has proved that the same investigator's experiments on the action of this drug on the circulation were made before the drug was absorbed, the same fallacy may exist here.

* *Bulletin de l'Acad. de Méd.*, 1877, p. 697.

† *Zur Wirkung des Salicylsäure*. Jena, 1875.

Gedl,* who gave man doses varying from 46 to 78 grains, found that in two cases there was no result, in three a lessening in the daily alterations in temperature, in three a slight fall of temperature, and in one a decided fall of 0.8° C.

Danilewsky states that the effects of the drug are slight and inconstant, while Mr. North† found that the acid prevented very powerfully the rise of temperature following severe exercise.

Notwithstanding the somewhat contradictory results obtained by these experiments, I think the bulk of evidence points to a reduction of normal temperature under the influence of this drug, and that there is no doubt but that salicylic acid in very large doses decreases temperature very greatly.

I report the following experiments in detail :

Experiment 1.—Rabbit ; weight, 2 pounds. Black doe.

Time. P.M.	Drug.	Rec. temp.	Remarks.
12.25		$102\frac{2}{3}^{\circ}$	
12.30	1 gr.		
12.55		102°	
1.15		$101\frac{2}{3}^{\circ}$	Animal huddles closely to the other, and apparently feels cold.
1.35		102°	
1.55		$101\frac{1}{3}^{\circ}$	

Time.	Drug.	Rec. temp.	Remarks.
2.15		102°	
2.35		$102\frac{1}{3}^{\circ}$	
3.35		$102\frac{2}{3}^{\circ}$	Fall of temperature = $1\frac{1}{3}^{\circ}$ F.

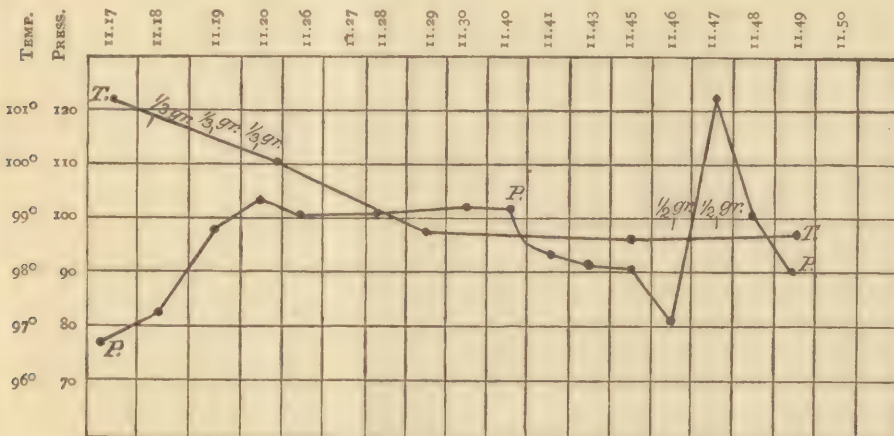
Experiment 2.—Rabbit ; weight, 2 pounds. White doe.

Time. P.M.	Drug.	Rec. temp.	Remarks.
3.40		$103\frac{1}{3}^{\circ}$	
3.45	1 gr.		Quiet.
4.05		103°	
4.25		102°	
5.25		$101\frac{2}{3}^{\circ}$	
5.45		$102\frac{2}{3}^{\circ}$	
6.05		$103\frac{1}{3}^{\circ}$	
6.25		$103\frac{1}{3}^{\circ}$	
6.45		$103\frac{2}{3}^{\circ}$	Fall of temperature $2\frac{1}{3}^{\circ}$ F.

Passing on to a consideration of the action of this acid on the circulation under normal conditions and in fever (ten experiments), we find that there seems to exist no relationship between arterial pressure and the temperature, and that under both conditions the drug causes a rise rather than a fall of pressure. On the abnormal or pyretic temperature salicylic acid in moderate or small doses seems to possess but little influence. Other observers, whose observations have been chiefly confined to the bedside, report that the drug has antipyretic powers, although even its most vehement supporters do not claim that it is very reliable as an antipyretic.

Charts showing Arterial Pressure and its Relationship to Temperature, also showing Fall of Temperature produced by Salicylic Acid.†

Experiment 3.—Rabbit ; weight, 3 pounds.



* *Centralblatt f. Med. Wissensch.*, 1876, p. 403.

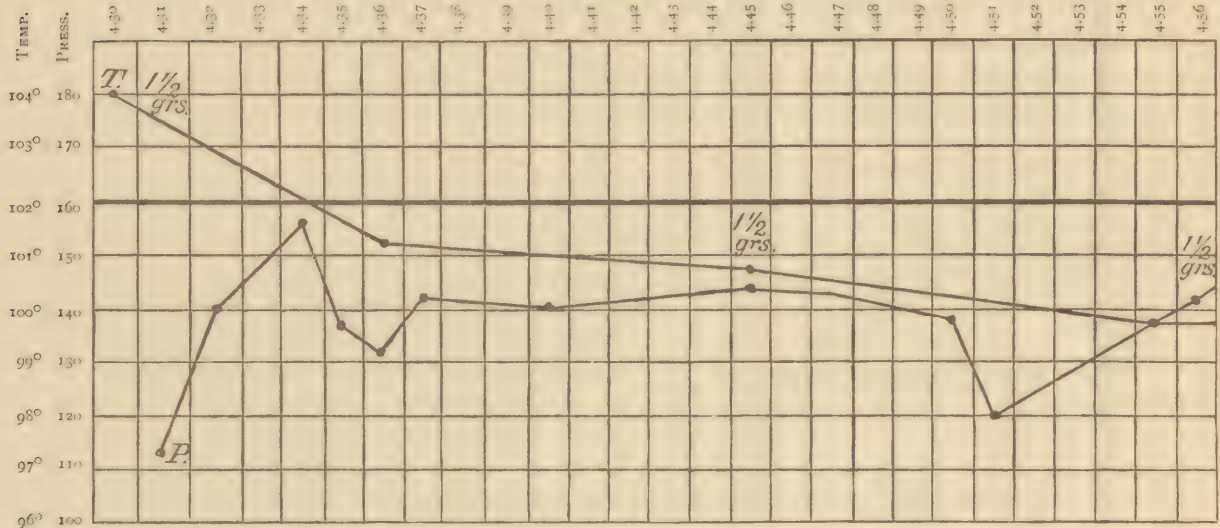
† *Practitioner*, xxiii. 184.

‡ It is proper to state that the details of many of the experiments have been left out owing to lack of space, not only in this portion of the paper but in the other portions also. In all, ninety experiments were performed, thirty on each drug.

Charts showing Arterial Pressure and its Relationship to Temperature, also showing Fall of Temperature produced by Salicylic Acid (Continued).

Experiment 4.—Dog ; weight, 12½ pounds.

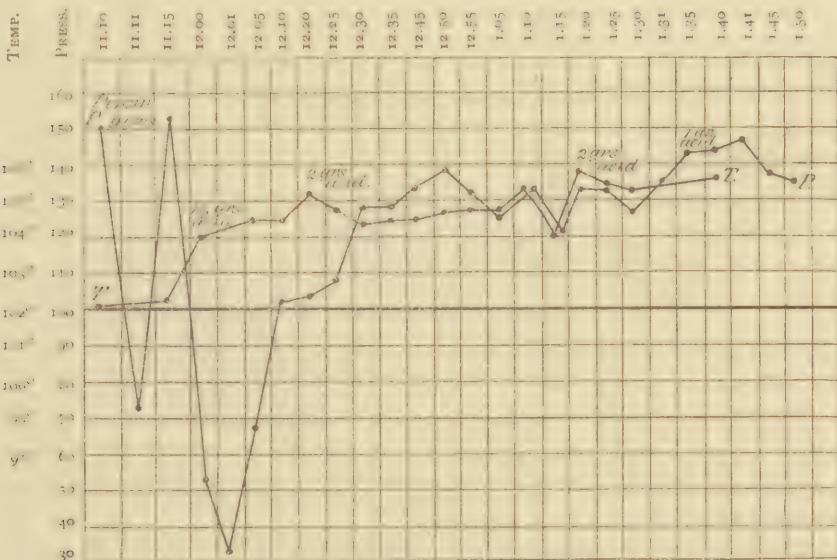
~~With Fever~~



With Fever

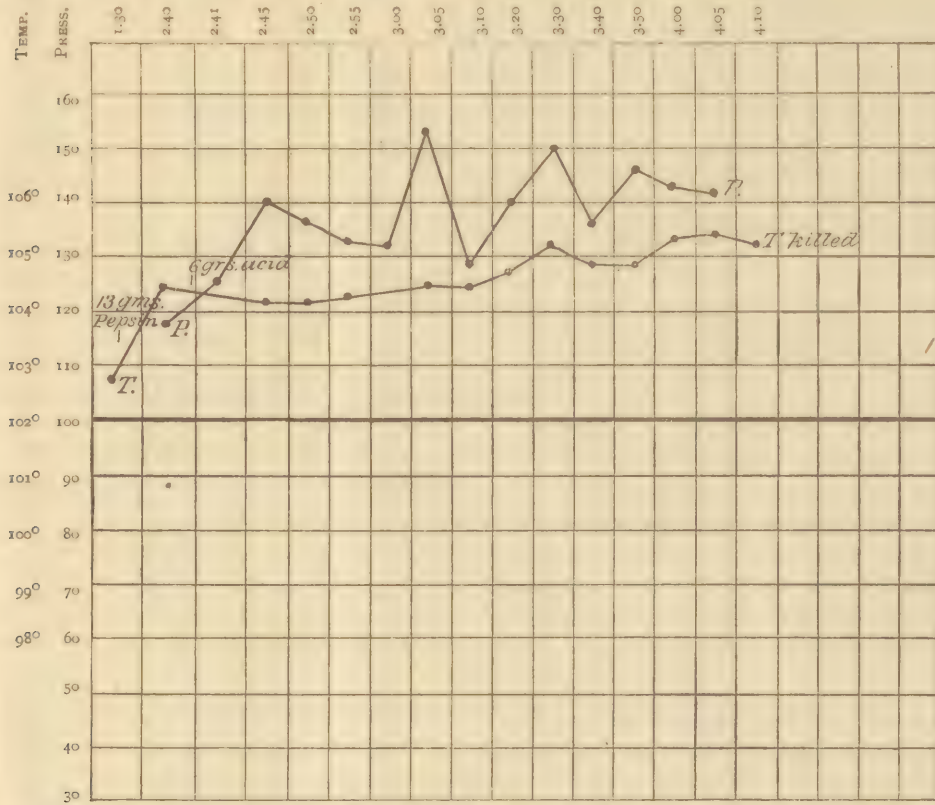
Rise of Temperature

Experiment 5.—Dog ; weight, 15 pounds.

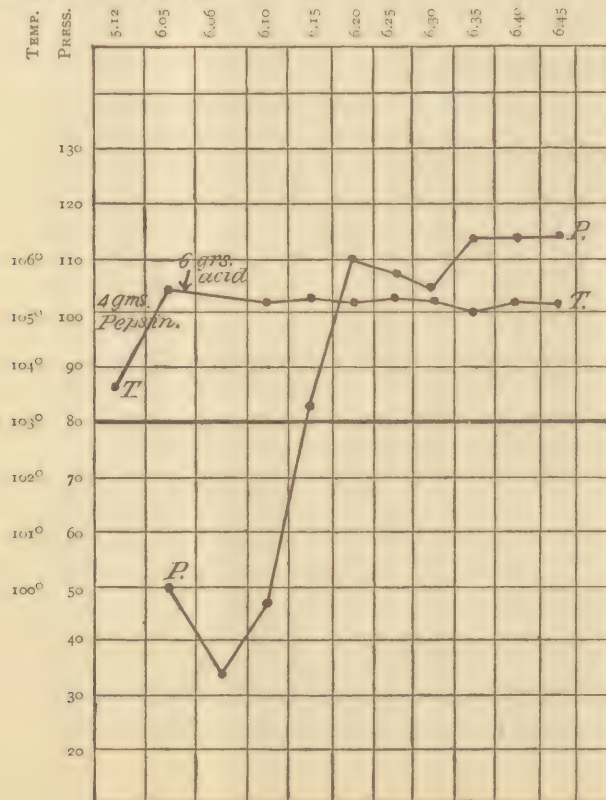


Charts showing Arterial Pressure and its Relationship to Temperature, also showing ~~Salicylic~~ effect
 Temperature produced by Salicylic Acid (Continued).

Experiment 6.—Dog; weight, 17 pounds.



Experiment 7.—Dog; weight, 32 pounds.



The study of the action of this drug on the production and dissipation of heat is the most interesting portion of its investigation, and a somewhat minute analysis of the results is therefore not out of place.

We find that in two experiments there was a *gain* of both dissipation and production, and that in the first of these the two functions balanced each other, while the second (No. 9) dissipation was very markedly increased over production.

In two other experiments there was a loss or decrease of both functions (Nos. 10 and 11).

In No. 10 dissipation was decreased more than was production, while in No. 11 heat production was decreased more than dissipation.

In No. 12 there was loss of dissipation and gain of production.

It will be seen, therefore, that the results obtained as to the method by which normal temperature is decreased are not concordant, but from the first four experiments it seems evident that the drug acts on both functions in reducing normal temperature.

Experiment 8.—Dog; weight, 20 pounds.

Time. A. M.	Rec. temp.	Box temp.
11.00	104.7°	55.20°
12.00		56.00°
1.00	104.6°	57.20°
	.1°	2.00°
1.15	4 grs. of salicylic acid into jugular.	
1.20	104.7°	57.05°
2.20		
3.20	104.6°	59.10°
	.1°	2.05°

Hourly dissipation of bodily heat..... 122.000
Hourly production of bodily heat..... 121.250

Hourly dissipation of heat after drug..... 125.050
Hourly production of heat after drug..... 124.300

SUMMARY.

Hourly dissipation of heat before drug..... 122.000
Hourly dissipation of heat after drug..... 125.050

Hourly gain* of dissipation..... 3.050

Hourly production of heat before drug..... 121.250
Hourly production of heat after drug..... 124.300

Hourly gain* of production 3.050

Experiment 9.—Dog; weight, 16 pounds.

Time. A. M.	Rec. temp.	Box temp.
11.00	103.0°	57.60°
12.00		
1.00	103.3°	58.90°
	.3°	1.30°
1.20	6 grs. of salicylic acid into jugular.	
1.30	104.3°	58.85°
2.30		
3.30	103.7°	60.25°
	.6°	1.40°

Hourly dissipation of bodily heat..... 79.300
Hourly production of bodily heat..... 81.100

Hourly dissipation of bodily heat after drug..... 85.400
Hourly production of heat after drug..... 81.800

SUMMARY.

Hourly dissipation of heat before drug..... 79.300
Hourly dissipation of heat after drug..... 85.400

Hourly gain of dissipation..... 6.100

Hourly production of heat before drug..... 81.100
Hourly production of heat after drug..... 81.800

Hourly gain of production..... .700

Experiment 10.—Dog; weight, 24 pounds.

Time. A. M.	Rec. temp.	Box temp.
10.55	103.7°	59.60°
11.55		60.60°
12.55	103.4°	61.25°
	.3°	1.65°
1.15	8 grs. of salicylic acid into jugular.	
1.25	103.7°	61.05°
2.25		
3.25	103.6°	62.05°
	.1°	1.00°

Hourly dissipation of bodily heat..... 100.650
Hourly production of bodily heat..... 97.950

Hourly dissipation after drug 61.000
Hourly production after drug..... 60.100

SUMMARY.

Hourly dissipation before drug..... 100.650
Hourly dissipation after drug..... 61.000

Hourly loss† of dissipation..... 39.650

Hourly production before drug..... 97.950
Hourly production after drug..... 60.100

Hourly loss† of production..... 37.805

Experiment 11.—Dog; weight, 23 pounds.

Time. A. M.	Rec. temp.	Box temp.
11.30	102.7°	58.45°
12.30		59.95°
1.30	103.7°	61.10°
	1.0°	2.65°

* The word "gain" is used here as synonymous with increase.

† The word "loss" is used as synonymous with decrease.

Time. P.M.		
1.40	8 grs. salicylic acid into jugular.	
1.55	103.0°	61°
2.55		...
3.55	103.4°	63°
	.4°	2°

Hourly dissipation of bodily heat.....	161.650
Hourly production of bodily heat.....	170.275
Hourly dissipation of heat after drug.....	122.000
Hourly production of heat after drug	123.100

SUMMARY.

Hourly dissipation before drug.....	161.650
Hourly dissipation after drug.....	122.000

Hourly loss of dissipation after drug.....	39.650
Hourly production of heat before drug.....	170.275
Hourly production of heat after drug.....	123.100
Hourly loss of production after drug	47.175

Experiment 12.—Dog ; weight, 35 pounds.

Time. A.M.	Rec. temp.	Box temp.
10.10	104.7°	61.95°
11.10		
12.10	104.1°	66.05°
	.6°	4.1°
12.28	8 grs. of salicylic acid into jugular.	
12.35	104.1°	65.95°
1.35		
2.35	104.7°	69.90°
	.6°	3.95°

Hourly dissipation of bodily heat.....	250.100
Hourly production of bodily heat.....	242.225
Hourly dissipation of heat after drug.....	240.950
Hourly production of heat after drug	248.825

SUMMARY.

Hourly dissipation of heat before drug.....	250.100
Hourly dissipation of heat after drug.....	240.950

Hourly loss of heat dissipation after drug.	9.150
Hourly production of heat before drug.....	242.225
Hourly production of heat after drug.....	248.825
Hourly gain of heat production after drug.	6.600

On analyzing the calorimetrical observations during fever we find that in one instance (No. 13) we have a gain of both functions, but that dissipation being increased more than was production, temperature was decreased thereby. In No. 14 both functions were decreased, but that production was decreased far more than was dissipation, thereby permitting a fall of temperature.

Again, in No. 15 dissipation was not influenced, while production was decreased.

In No. 16 there was loss of both functions, dissipation being more decreased than production.

In No. 17 the same condition of affairs also held.

These results are much more discordant than those obtained on normal temperature, and agree with the experiments already given, showing that the drug does not have any positive power over fever.

Thus, in one instance, the fall of temperature depended on increased dissipation, and in two others on decreased production, while in the remaining experiments there was a rise in temperature due to a greater failure of dissipation than production.

Experiment 13.—Dog ; weight, 12 pounds.

3.45 Rec. temp. 105°. Gave 1 grm. pepsin into jugular.

Time. A.M.	Rec. temp.	Box temp.
4.20	105.8°	66.30°
5.20	107.9°	66.50°
	2.1°	.20°
5.22	5 grs. salicylic acid into jugular.	
5.25	107.5°	66.30°
6.25	105.8°	66.80°
	1.7°	.50°

Hourly dissipation of heat before acid	24.400
Hourly production of heat before acid	43.300
Hourly dissipation of heat after acid.....	61.000
Hourly production of heat after acid.....	45.700

SUMMARY.

Hourly dissipation of heat before drug.....	24.400
Hourly dissipation of heat after drug	61.000

Hourly gain of dissipation after drug.....	36.600
Hourly production of heat before drug.....	43.300
Hourly production of heat after drug	45.700

Hourly gain of production after drug..... 2.400

Result.—Gain of both dissipation and production, the dissipation being increased the more.

Experiment 14.—Dog ; weight, 24½ pounds.

10.30 Rec. temp. 103°. Injected 3 grms. filtered pepsin.

Time. A.M.	Rec. temp.	Box temp.
11.10	103.7°	61.15°
12.10	105.3°	62.45°
	1.6°	1.30°
12.25	Injected 6 grs. salicylic acid into jugular.	
12.30	105.0°	62.35°
1.30	105.2°	63.50°
	.2°	1.15°

Hourly dissipation of heat.....	158.600
Hourly production of heat.....	188.300
Hourly dissipation after drug.....	130.300
Hourly production after drug.....	133.670

SUMMARY.

Hourly dissipation of heat before drug.....	158.600
Hourly dissipation of heat after drug.....	130.300
Hourly loss of dissipation after drug....	28.300
Hourly production of heat before drug.....	188.300
Hourly production of heat after drug.....	133.670
Hourly loss of production after drug....	54.630

Result.—Loss of both functions, production being very markedly lessened.

Experiment 15.—Dog; weight, 12 pounds.

12.40 Rec. temp. 104.2°. Injected 3 grms. pepsin.

Time. P. M.	Rec. temp.	Box temp.
1.35	107.15°	63.35°
2.35	107.80°	63.70°
	.65°	.35°
2.37	6 grs. salicylic acid into jugular.	
2.40	106.70°	63.45°
3.40	107.10°	63.80°
	.40°	.35°

Hourly dissipation of heat.....	42.700
Hourly production of heat.....	48.550
Hourly dissipation after drug.....	42.700
Hourly production after drug.....	46.300

SUMMARY.

Hourly dissipation before drug.....	42.700
Hourly dissipation after drug.....	42.700

Hourly dissipation after drug unchanged.

Hourly production of heat before drug.....	48.550
Hourly production of heat after drug.....	46.300

Hourly loss of production after drug..... 2.250

Result.—Loss of production. Dissipation not affected.

Experiment 16.—Dog; weight, 22½ pounds.

Time. P. M.	Rec. temp.	Box temp.
3.45	104.5°	63.55°
4.45	104.8°	64.55°
	.3°	1.00°
4.47	Injected 6 grs. salicylic acid.	
4.50	104.5°	64.00°
5.50	104.9°	64.85°
	.4°	.85°

Hourly dissipation of heat.....	122.0000
Hourly production of heat.....	127.1625
Hourly dissipation after drug.....	103.7000
Hourly production after drug.....	110.4500

SUMMARY.

Hourly dissipation before drug.....	122.000
Hourly dissipation after drug.....	103.700

Hourly loss of dissipation after drug... 17.300

Hourly production of heat before drug.....	127.1625
Hourly production of heat after drug.....	110.4500

Hourly loss of production after drug... 16.7125

Result.—Loss of both. Greater loss of the two is in dissipation.

Experiment 17.—Dog; weight, 19½ pounds.

10.15 Rec. temp. 103.7°. Injected 3 grms. of pepsin filtered.

Time. A. M.	Rec. temp.	Box temp.
11.00	104.7°	62.45°
12.00	104.6°	63.40°
	.1°	.95°
12.02	6 grs. salicylic acid into jugular.	
12.15	103.7°	63.25°
1.15	104.7°	64.00°
	1.0°	.75°

Hourly dissipation of heat.....	115.900
Hourly production of heat.....	114.438

Hourly dissipation of heat after drug.....	91.500
Hourly production of heat after drug.....	106.125

SUMMARY.

Hourly dissipation of heat before drug.....	115.900
Hourly dissipation of heat after drug.....	91.500

Hourly loss of dissipation after drug.... 24.400

Hourly production of heat before drug.....	114.438
Hourly production of heat after drug.....	106.125

Hourly loss of production after drug.... 8.313

Result.—Loss of dissipation and production, the loss of dissipation being the greater.

A SUMMARY OF THE ACTION OF SALICYLIC ACID ON BODILY TEMPERATURE.

1. *Salicylic acid* has the power to reduce slightly normal bodily heat.

2. *Salicylic acid*, according to the writer's experiments, has but little power over pyretic temperature.

3. *Salicylic acid*, when acting on either normal or abnormal temperature, does not seem to have much influence on the circulation either in regard to pulse-rate or arterial pressure. Any change, when it occurs, seems to be an increase of arterial pressure rather than a decrease, and this increase occurred more markedly in the normal than in the pyretic animal.

4. *Salicylic acid*, in reducing normal temperature, probably acts on both functions, namely, production and dissipation, while it seems to act very uncertainly and irregularly when reducing high temperature, failing frequently, as before stated, to prevent an increase of bodily heat.

III. CARBOLIC ACID.*

THE influence of carbolic acid on temperature in the normal animal has not, that I am aware of, been studied, although Emil Erls† has found that in mild putrid poisoning it greatly diminishes fever heat, but if the poisoning be severe the acid has no influence.

On glancing at the following tables, which represent the results reached in a series of ten experiments on the normal rectal temperature of rabbits, it is evident that this drug acts much more positively than does salicylic acid, and we find that in every instance there was a fall in the normal bodily heat after the administration of the drug, though in one instance this fall ultimately ended in a rise, which passed above the original and primary temperature of the animal before the injection of the acid.

Experiment 1.—Rabbit; weight, 3 pounds. Gray doe.

Time. A.M.	Drug.	Rec. temp.	Remarks.
11.35		102 $\frac{2}{3}$ °	
11.37	3 drops.		Struggled hard when caught.
11.57		103°	Drug injected hypodermically in 30 minims of glycerin and water.
12.17		102 $\frac{3}{5}$ °	
12.37		101 $\frac{1}{5}$ °	
12.57		101 $\frac{1}{5}$ °	
1.17		101 $\frac{1}{5}$ °	
1.37		101 $\frac{1}{5}$ °	
1.57		101 $\frac{2}{5}$ °	
2.17		101 $\frac{1}{5}$ °	
2.37		101°	
6.15		101 $\frac{1}{5}$ °	Fall of temperature 1 $\frac{2}{5}$ ° F.

* The carbolic acid used was made by Calvert and was chemically pure, and consisted of the drops obtained from deliquescence of the crystals.

† *Schmidt's Jahrbücher*, Bd. clxiv. p. 148.

Experiment 2.—Rabbit; weight, 2 pounds. Black and white doe.

Time. A.M.	Drug.	Rec. temp.	Remarks.
11.15		103 $\frac{2}{3}$ °	
11.17	2 drops.		Quiet.
12.05		102°	Injected hypodermically in 30 minims of glycerin and water.
12.35		101 $\frac{1}{5}$ °	
1.05		102 $\frac{1}{5}$ °	
1.35			
2.05		102 $\frac{1}{5}$ °	
3.00		102 $\frac{4}{5}$ °	Fall of temperature = 1 $\frac{4}{5}$ ° F.

Experiment 3.—Rabbit; weight, 2½ pounds. Black doe.

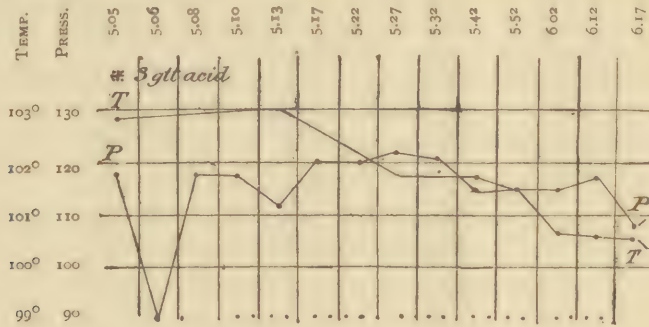
Time. A.M.	Drug.	Rec. temp.	Remarks.
10.55		103 $\frac{2}{5}$ °	
10.56	2½ drops.		Injected hypodermically in 30 minims of glycerin and water.
11.15		102°	
11.35		102°	
12.05		101 $\frac{3}{5}$ °	
12.40		101 $\frac{4}{5}$ °	
1.10		102 $\frac{2}{5}$ °	
1.40		102 $\frac{4}{5}$ °	Fall of temperature = 1 $\frac{1}{5}$ ° F.

These results are likewise supported by the experiments performed to determine the relation between the arterial pressure and the temperature in the normal animal (dogs), in all five of which a fall of temperature occurred. I think we may, therefore, consider proven that this acid lowers normal bodily temperature.

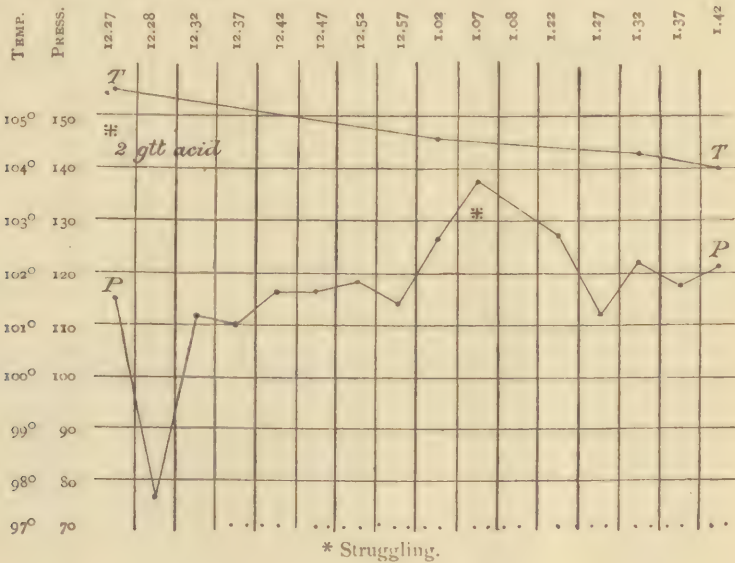
The charts showing the relationship between arterial pressure and the lowering of normal temperature by this drug indicate, at least in part, that there is a fall of pressure *pari passu* with the temperature, although in two of the five experiments the fall of arterial pressure was but momentary, and was followed by a rise. I can give no explanation of this variation. (Two charts left out for want of space.)

Charts showing Arterial Pressure and its Relationship to Temperature, also showing Fall of Temperature produced by Carbolic Acid when that Temperature is Normal.

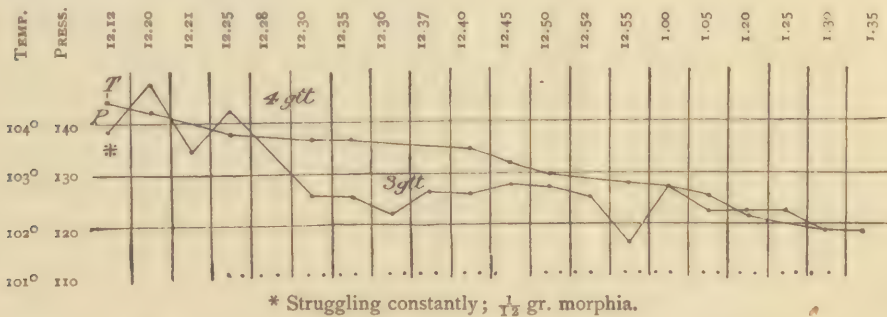
Experiment 4.—Dog ; weight, 14 pounds.



Experiment 5.—Dog ; weight, 30 pounds.



Experiment 6.—Dog ; weight, 42 pounds.

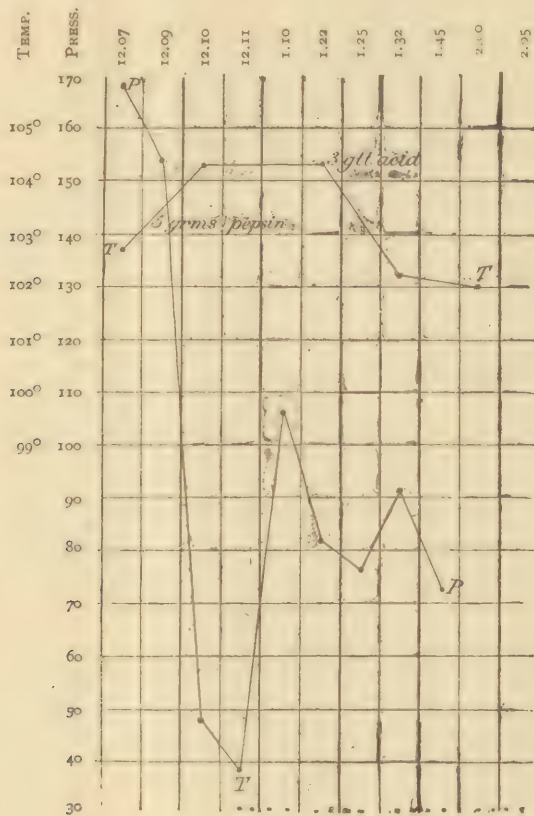


On examining the charts showing the influence of carbolic acid on fever, and the relationship existing between arterial pressure and temperature in fever, we note that in three of the five experiments there was a marked fall of temperature, while in the remaining two there was a rise, or, in other

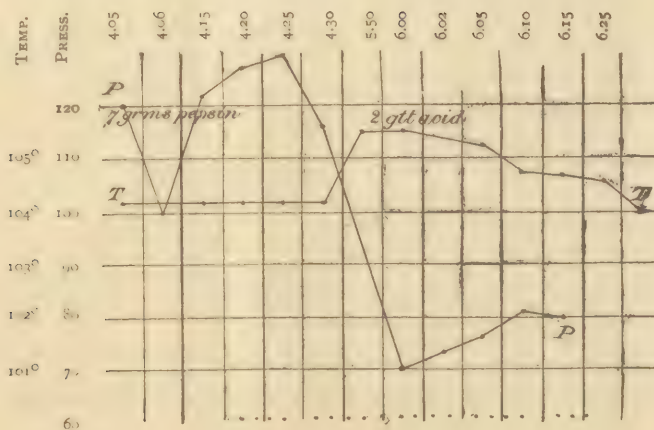
words, the drug failed to control the pyrexia. In three of the experiments there was a fall of arterial pressure with a fall of temperature, in one there was a rise in pressure with a fall of temperature, and in another there was a fall in pressure with a rise in temperature. (One chart left out for want of space.)

Charts showing the Relationship between Arterial Pressure and Temperature under the Influence of Carbolic Acid in Pepsin Fever.

Experiment 7.—Dog ; weight, 19 pounds.



Experiment 8.—Dog ; weight, 25 pounds.

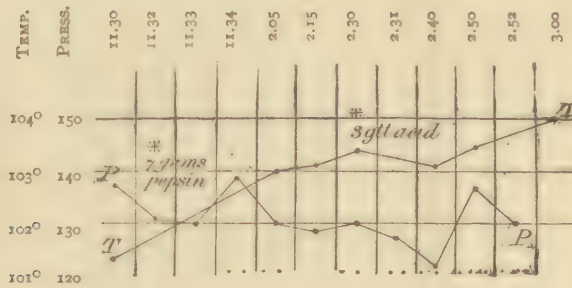


Charts showing the Relationship between Arterial Pressure and Temperature under the Influence of Carbolic Acid in Pepsin Fever (Continued).

Experiment 9.—Dog; weight, 26 pounds.



Experiment 10.—Dog; weight, 20 pounds.



Notwithstanding the fact that the two last named experiments conflict with the first three, I think that we may say that carbolic acid in lowering pyretic temperatures likewise lowers arterial pressure, and this view is strengthened by the results of the experiments performed on normal temperature.

Calorimetrical experiments made to determine in what manner carbolic acid lowers normal bodily temperature are, as might be expected from the irregular results obtained in the experiments just detailed, not very satisfactory.

It will be noted that in some instances production or dissipation were affected alone or together, while in others one function was decreased while the other was increased.

As the writer used the greatest care in the performance of the experiments there is but little room for fallacy, and, in view of the irregular action of the drug, it would seem probable that it possesses no particular influence on either function, but may reduce temperature in some instances by acting on both functions.

Experiment 11.—Dog; weight, 18 pounds.

Time, P.M.	Rec. temp.	Box temp.
3.10	103.6°	57.00°
4.10	105.0°	57.95°
	1.4°	.95°
4.15	3 drops carbolic acid into jugular.	
4.25	104.5°	58.05°
5.25	105.2°	59.40°
	.7°	1.35°

Hourly dissipation of bodily heat.....	115.900
Hourly production of bodily heat.....	134.800
Hourly dissipation of heat after drug.....	164.700
Hourly production of heat after drug.....	174.150

SUMMARY.

Hourly dissipation of heat before drug.....	115.900
Hourly dissipation of heat after drug.....	164.700
Hourly gain of dissipation after drug....	48.800
Hourly production of heat before drug.....	134.800
Hourly production of heat after drug	174.150
Hourly gain of production after drug....	39.350

Result.—Gain of both functions, dissipation being most increased.

Experiment 12.—Dog ; weight, 14.5 pounds.

Time. A.M.	Rec. temp.	Box temp.
10.35	102.7°	59.55°
1.50	103.0°	61.08°
	.3°	1.53°
1.55	3 drops of carbolic acid into jugular.	
2.00	102.7°	61.75°
5.15	103.6°	63.35°
	.9°	1.60°

Hourly dissipation of bodily heat.....	57.43400
Hourly production of bodily heat.....	58.43784
Hourly dissipation after drug	60.06152
Hourly production after drug	63.07304

SUMMARY.

Hourly dissipation of heat before drug.....	57.43400
Hourly dissipation of heat after drug.....	60.06152
Hourly gain of dissipation after drug...	2.62752
Hourly production of heat before drug.....	58.43784
Hourly production of heat after drug.....	63.07304

Hourly gain of production after drug... 4.63520

Result.—Gain of both functions, production being most increased.

Experiment 13.— Dog ; weight, 29.5 pounds.

Time. A.M.	Rec. temp.	Box temp.
10.35	103.5°	55.65°
11.35	103.6°	56.70°
	.1°	1.05°
11.55	4 drops carbolic acid into jugular.	
12.00	104.0°	56.50°
1.00	104.1°	57.40°
	.1°	.90°

Hourly dissipation of heat.....	128.100
Hourly production of heat.....	129.575
Hourly dissipation of heat after drug.....	109.800
Hourly production of heat after drug.....	111.275

SUMMARY.

Hourly dissipation of heat before drug.....	128.100
Hourly dissipation of heat after drug.....	109.800
Hourly loss of dissipation after drug...	18.300
Hourly production of heat before drug.....	129.575
Hourly production of heat after drug.....	111.275

Hourly loss of production after drug..... 18.300

Result.—Loss of both functions equally.

Experiment 14.—Dog ; weight, 22 pounds.

Time. P.M.	Rec. temp.	Box temp.
1.15	103.4°	57.20°
2.15	103.5°	58.45°
	.1°	1.25°
2.40	4 drops carbolic acid into jugular.	
2.45	103.4°	57.95°
3.45	103.3°	58.85°
	.1°	.90°

Hourly dissipation of bodily heat.....	155.500
Hourly production of bodily heat.....	157.150
Hourly dissipation after drug	109.800
Hourly production after drug	108.250

SUMMARY.

Hourly dissipation before drug.....	155.500
Hourly dissipation after drug	109.800
Hourly loss of dissipation after drug....	45.700
Hourly production of heat before drug.....	157.150
Hourly production of heat after drug.....	108.250

Hourly loss of heat production after drug. 48.900

Result.—Loss of both functions, production being the more decreased.

Experiment 15.—Dog ; weight, 25 pounds.

Time. P.M.	Rec. temp.	Box temp.
3.50	105.5°	59.15°
4.50	104.6°	60.30°
	.9°	1.15°
4.55	4 drops carbolic acid into jugular.	
5.00	104.6°	60.00°
6.00	105.7°	60.90°
	1.1°	.90°

Hourly dissipation of heat before drug.....	140.300
Hourly production of heat before drug.....	123.425
Hourly dissipation of heat after drug.....	109.800
Hourly production of heat after drug.....	130.425

SUMMARY.

Hourly dissipation of heat before drug.....	140.300
Hourly dissipation of heat after drug.	109.800
Hourly loss of dissipation after drug.....	30.500
Hourly production of heat before drug.....	123.425
Hourly production of heat after drug.....	130.425

Hourly gain of production after drug... 7.000

Result.—Loss of dissipation, gain of production.

The results obtained in the calorimetrical study of this acid on fevered animals are more concordant than those reached in the study on normal dogs, for we find that in Experiments 16, 18, and 19 heat production is very positively decreased, while in every instance where there was no decrease in production there was an increase in dissipation, which, while it did not always amount to a large enough quantity to overcome an increased production, had an effect in lessening the rise in temperature which might come on.

In one experiment, however (No. 20), production was very greatly increased over dissipation, simply because the thermogenic agent caused a rise in temperature which the acid could not affect. It would seem from these experiments that the acid lowers temperature by acting on both heat production and dissipation, the production being generally most affected.

Experiment 16.—Dog; weight, 21 pounds.

11.25 Rec. temp. 103.7°. Injected 2 grms. filtered pepsin.

Time. P.M.	Rec. temp.	Box temp.
12.02	105.0°	57.00°
1.02	104.7°	58.40°
	.3°	1.40°
1.05	3 gtt. of carbolic acid into jugular.	
1.10	104.8°	58.85°
2.10	102.8°	59.65°
	2.0°	.80°

Hourly dissipation of heat.....	170.800
Hourly production of heat.....	166.075
Hourly dissipation of heat after drug.....	97.600
Hourly production of heat after drug.....	66.100

SUMMARY.

Hourly dissipation of heat before drug.....	170.800
Hourly dissipation of heat after drug.....	97.600
Hourly loss of dissipation after drug.....	73.200
Hourly production of heat before drug.....	166.075
Hourly production of heat after drug.....	66.100
Hourly loss of production after drug.....	99.975

Result.—Loss of both dissipation and production.
Loss of production very great.

Experiment 17.—Dog; weight, 16 pounds.

10.35 Rec. temp. 103.5°. Injected 2 grms. filtered pepsin.

Time. P.M.	Rec. temp.	Box temp.
2.15	105.2°	59.85°
3.00	104.1°	60.06°
	1.1°	.21°
3.01	3 drops of carbolic acid injected into jugular.	
3.12	104.0°	60.80°
3.57	103.1°	61.35°
	.9°	.55°

Hourly dissipation of heat.....	32.025
Hourly production of heat.....	15.525
Hourly dissipation after drug.....	83.875
Hourly production after drug.....	70.375

SUMMARY.

Hourly dissipation of heat before drug.....	32.025
Hourly dissipation of heat after drug.....	83.875
Hourly gain of dissipation after drug.....	51.850
Hourly production of heat before drug.....	15.525
Hourly production of heat after drug.....	70.375
Hourly gain of production after drug.....	54.850

Result.—Gain of both dissipation and production, production being affected most.

Experiment 18.—Dog; weight, 34 pounds.

1.40 Rec. temp. 104°. Injected 2 grms. filtered pepsin.

Time. P.M.	Rec. temp.	Box temp.
4.00	105.6°	61.50°
5.00	105.7°	62.95°
	.1°	1.45°
5.02	Injected 4 gtt. of carbolic acid into jugular.	
5.20	105.6°	62.95°
6.20	104.0°	64.05°
	1.6°	1.10°

Hourly dissipation of heat.....	176.900
Hourly production of heat.....	179.450
Hourly dissipation after drug.....	134.200
Hourly production after drug.....	93.400

SUMMARY.

Hourly dissipation before drug.....	176.900
Hourly dissipation after drug.....	134.200
Hourly loss in dissipation after drug.....	42.700
Hourly production of heat before drug.....	179.450
Hourly production of heat after drug.....	93.400
Hourly loss of production after drug....	86.050

Result.—Both functions decreased, the production being greatly decreased.

Experiment 19.—Dog; weight, 14½ pounds.

10.30 Rec. temp. 102.2°. Injected 1 gm. filtered pepsin.

Time. A.M.	Rec. temp.	Box temp.
10.50	104.0°	57.85°
11.50	103.5°	58.80°
	.5°	.95°
11.53	3 gtt. carbolic acid injected into jugular.	
11.55	103.5°	58.75°
12.55	99.0°	59.70°
	4.5°	.95°

Hourly dissipation of heat.....	115.9000
Hourly production of heat.....	110.4625
Hourly dissipation after drug.....	115.9000
Hourly production after drug.....	66.9625

SUMMARY.

Hourly dissipation before drug.....	115.9000
Hourly dissipation after drug.....	115.9000
Hourly dissipation after drug unchanged.	
Hourly production before drug.....	110.4625
Hourly production after drug.....	66.9625
Hourly loss of production after drug...	43.5000

Result.—Dissipation not affected. Production greatly decreased.

Experiment 20.—Dog ; weight, 28 pounds.

2.10 Rec. temp. 103°. Injected 2 grms. filtered pepsin.

Time. P. M.	Rec. temp.	Box temp.
3.15	104.2°	60.00°
4.15	104.7°	61.65°
	.5°	1.65°
4.18	3 gtt. carbolic acid into jugular.	
4.20	104.6°	61.60°
5.20	106.3°	63.50°
	1.7°	1.90°

Hourly dissipation of heat..... 203.300
Hourly production of heat..... 213.800

Hourly dissipation after drug..... 231.800
Hourly production after drug..... 288.500

SUMMARY.

Hourly dissipation of heat before drug..... 203.300
Hourly dissipation of heat after drug..... 231.800

Hourly gain of dissipation after drug.... 28.500

Hourly production of heat before drug..... 213.800
Hourly production of heat after drug..... 288.500

Hourly gain of production after drug 74.700

Result.—Both increased, production being more increased than dissipation by a considerable amount.

CONCLUSIONS.

1. Carbolic acid possesses considerable power in lowering normal bodily temperature.
2. It possesses more influence over pyretic temperature than does salicylic acid, generally preventing a rise or causing a fall of temperature, but sometimes failing to do so.
3. Carbolic acid probably decreases arterial pressure when lowering temperature.
4. That its mode of decreasing normal bodily temperature is as yet not fully understood, although it would seem probable that it acts on both heat functions.
5. When influencing bodily heat in fever it acts chiefly by decreasing production, although it affects both functions.

This study of the action of certain drugs on bodily heat, as originally carried out, consisted of thirty experiments, on each of the drugs named, divided in the following manner:

1. Ten experiments to determine the effect of the drug on normal rectal temperature.
2. Five experiments to determine the effect of the drug on normal temperature and arterial pressure.
3. Five similar experiments on *pyretic* temperature and arterial pressure.
4. Five experiments on the influence of the drug on the production and dissipation of heat in the normal animal, and five similar experiments on the fevered animal.

Owing to the lack of space in the THERAPEUTIC GAZETTE, where this paper first appeared, and from which this reprint is taken, the records of thirty-three experiments were necessarily left out, while many minor details belonging to the whole paper were also excluded.

